Office Action Summary	Application No.	Applicant(s)
	10/564,769	ONICHTCHOUK ET AL.
	Examiner	Art Unit
	MARIANNE P. ALLEN	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-59 and 63-67* is/are pending in the application.

4a) Of the above claim(s) *40-49,51-57 and 59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50,58 and 63-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *40-59 and 63-67* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☐ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.	6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed 5/24/11 have been fully considered but they are not persuasive.

Claims 1-39 and 60-62 have been cancelled. Claims 66-67 have been newly added. Claims 63-65 have been amended to depend on claim 58 (the elected invention).

Election/Restrictions

Claims 40-49, 51-57, and 59 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/22/10.

Claims 50, 58, and 63-67 are under consideration by the examiner.

Specification

The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

Although applicant's 5/24/11 response includes an abstract, the response only requests that it be incorporated into the specification. It does not make clear that the abstract remains on a separate sheet, apart from any other text.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 50, 63, and 66-67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 50, 63, and 66-67 are not original claims and basis for these claims is not apparent.

There is no basis for treating any metabolic disease or metabolic dysfunction as recited in claim 50. The specification discloses particular metabolic diseases such as diabetes and particular metabolic dysfunctions such as metabolic syndrome.

Claim 63 part (a) is directed to isoforms, fragments or variants of SEQ ID NO: 2. The specification does not disclose nor define variants. Furthermore, parts (e) and (f) permit mutated forms of these isoforms and variants. There is no basis for this concept.

There is no basis for claim 66-67 in claim 48 (not an original claim itself) and paragraphs [80, 87]. There is no disclosure of contacting a cell that expresses an unspecified pancreatic gene with an effective amount of human pleiotrophin polypeptide to produce insulin producing β cells. Note that the cell being contacted does not need to be a β cell (insulin producing or otherwise). Claim 66 can be any cell and claim 67 can be any pluripotent stem cell.

Claims 50, 58, and 63-67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The examples indicate that human pleiotrophin was expressed in a mouse embryonic stage 9.5-15 pancreatic bud library. Its expression was determined in various tissues of wild-type, fasted, and ob/ob (genetically obese) mice. Its expression was determined in mice on a high fat diet. (See at least Figures 2A-C.)

Example 8 discloses that in vitro, stable mouse embryonic stem (ES) cells expressing Pax4 were generated. Pax4 and wild type ES cells were cultured to allow the formation of embryoid bodies. Embryoid bodies were subsequently plated, enzymatically dissociated, and replated. After dissociation, cells were cultured in a differentiation medium containing various growth factors. Additionally DG001 enriched supernatant of 293 cells was added every second day until day 40. Under such conditions, the expression of insulin was induced by DG001 (Fig. 3). The results shown in Figure 3 demonstrate a significant induction of the differentiation of insulin-producing cells, if DG001 is added in later stages of differentiation.

Examples 9 and 10 are prophetic and do not disclose any experiments actually performed.

The specification does not disclose nor exemplify administering DG001 polypeptide or a functional fragment thereof to treat any disease or condition embraced by the claims. No regeneration of any pancreatic cells or tissues is exemplified. No modulation of pancreatic development in a subject is exemplified. No production of insulin producing β cells from any cell or any pluripotent stem cell is exemplified.

Claim 50 is directed to treating diabetes, obesity, metabolic syndrome, any metabolic disease, and any metabolic dysfunction by administering a human pleiotrophin polypeptide or a functional fragment thereof.

Claim 58 is directed to the treatment, alleviation or prevention of diabetes, obesity, or metabolic syndrome, or modulation of pancreatic development, or regeneration of pancreatic cells or tissues by administering a human pleiotrophin polypeptide or a functional fragment thereof.

Claim 66 is directed to a method for generating insulin producing β cells comprising contacting a cell that expresses a pancreatic gene with a human pleiotrophin polypeptide. The claims as written are not clearly in vivo or in vitro and are interpreted to embrace both situations. It is noted that Example 8 does not produce insulin producing β cells. It is not clear what changes, attributes, and/or characteristics would need to be found in the treated cell or pluripotent stem cell in order to meet the limitation of "insulin producing β cells." It is not known what expressed pancreatic genes would produce the claimed results.

Neither claim 50 nor claim 58 requires any specific outcome from the treatment. As such, the claims are interpreted as including prevention and cure of all recited conditions and treatment of all aspects of the recited conditions. The specification does not disclose that human pleiotrophin or fragments thereof could be used to prevent or cure any disease embraced by the claims. There is no evidence or reason to believe that human pleiotrophin would have this effect.

Claim 50 is interpreted as including treating all metabolic diseases such as phenylketonuria (PKU) and porphyria.

Claims 50 and 58 are interpreted as including treating all causes of obesity including Cushing's syndrome and polycystic ovary syndrome (PCOS).

Claims 50 and 58 are interpreted as including treating all aspects of metabolic syndrome including hypertension and high blood lipid levels.

The specification does not establish that human pleiotrophin or fragments thereof can be used to treat, prevent, or cure any of these conditions. There is no evidence nor reason to believe that adminstering a human pleiotrophin polypeptide would treat these conditions. Note that the "subject" is not limited to humans or mammals but includes any suitable subject. There is no evidence that human pleiotrophin would have any effect on a subject such as a sloth, a whale, or a snake.

Claims 50, 58, 63, and 65-67 are not limited to the protein of SEQ ID NO: 2. It is not known what the structure of a **functional** fragment of a human pleiotrophin polypeptide would be. The particular function required is not specified. The specification provides no results on fragments or isoforms of SEQ ID NO: 2. The specification does not identify the portion of SEQ ID NO: 2 that is responsible for the claimed activity.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or

absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

The present claims are an invitation to experiment and would require undue experimentation. The breadth of the claims is large and there are no working examples that would correlate to the claimed methods of treatment. It is not considered to be so predictable that the in vitro results of Example 8 could be extrapolated to enable the claimed methods.

Applicant's arguments and the case law cited are not persuasive. The specification and prior art of record do not establish that any experimental system or results in the examples correlate to or would have been understood by one of ordinary skill in the art at the time of the invention to be a model system representative of any or all of the diseases embraced by the claims. The **known** or **recognized** correlation of an in vitro system or in vivo model system to the claimed in vivo medical conditions underlies all of the case law relied upon by applicant. In the case law cited by applicant these correlations were known or recognized by those of ordinary skill in the art. This known correlation is what is lacking in the instant application.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 65 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 65 is confusing in reciting that the diabetes is insulin dependent diabetes mellitus or non-insulin dependent diabetes mellitus. This appears to imply that there are other types of diabetes. It is not clear what applicant intends.

The following is a quotation of the fourth paragraph of 35 U.S.C. 112:

> Subject to the [fifth paragraph of 35 U.S.C. 112], a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

Claim 63 is rejected under 35 U.S.C. 112, 4th paragraph, as being of improper dependent form for failing to further limit the subject matter of the claim upon which it depends, or for failing to include all the limitations of the claim upon which it depends.

Claim 58 is directed to administering human pleiotrophin or a functional fragment. Claim 63 is dependent upon claim 58; however, it includes variants of the polypeptide of SEQ ID NO: 2 (see part (a)), sequences encoded by hybridizing polynucleotide sequences (see part (d)), and mutated sequences (see parts (e) and (f)). These are not considered to meet the limitation in claim 58 of a "human" pleiotrophin and are considered to embrace pleiotrophins from other species. Particularly with respect to variants, mutants, and homologous sequences, there are no sequence changes that are considered to retain the "human" aspect of the sequence. Once mutated the polypeptide is no longer naturally occurring and cannot be considered "human."

Applicant may cancel the claim(s), amend the claim(s) to place the claim(s) in proper dependent form, rewrite the claim(s) in independent form, or present a sufficient showing that the dependent claim(s) complies with the statutory requirements.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 50, 58, 63, 64, and 65 are rejected under 35 U.S.C. 102(e) as being anticipated by Colley et al. (U.S. Patent Publication 2003/0202960).

Colley et al. discloses using recombinant human pleiotrophin (PTN) as an angiogenic factor in treating heart disease (an aspect of diabetes), diabetic neurovasculopathy, and diabetic ulcers. The human PTN can be administerered to a human subject. See at least abstract, claims, and pages 1-4.

Note that claim 65 is directed to all forms of diabetes.

Applicant's arguments are unpersuasive. No particular outcome is required by the claims. No particular aspect of the disease is required to be treated by the claim. The prior art administers human pleiotrophin to a subject. This is the only step required by the claim.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is (571)272-0712. The examiner can normally be reached on Monday-Friday, 5:30 am - 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marianne P. Allen/
Primary Examiner, Art Unit 1647

mpa